

Anesthetic Management of a Child With Congenital Central Hypoventilation Syndrome (CCHS, Ondine's Curse) for Dental Treatment

Hajime Ishibashi, DDS, PhD,* Koji Umezawa, DDS, PhD,† Sachiyo Hayashi, DDS,† and Koh Shibutani, DDS, PhD*

*Department of Anesthesiology and †Department of Dentistry for the Disabled, Nihon University School of Dentistry at Matsudo, Chiba, Japan

Congenital Central Hypoventilation Syndrome (CCHS, also known as Ondine's Curse) is a rare syndrome characterized by apnea, cyanosis, and hypotonia. A 4-year-old, 90-cm, 12-kg girl with CCHS, mental retardation (MR), and Hirschsprung's disease (HD) was treated under general anesthesia. Intravenous drugs were not used, but sevoflurane, a volatile anesthetic, was used. As a result, the recovery time from the end of the operation to returning to the ward was very short, only 18 minutes. There was no trouble during the perioperative period. We safely performed general anesthesia and dental treatment for a girl who had CCHS with HD and MR.

Key Words: CCHS; Ondine's Curse; General anesthesia; Dental treatment.

Congenital Central Hypoventilation Syndrome (CCHS, also known as Ondine's Curse) is a rare syndrome characterized by apnea, cyanosis, and hypotonia.^{1,2} Hirschsprung's disease (HD) is a condition caused by congenital absence of ganglion cells from the enteric nervous system, resulting in bowel obstruction.¹

Here we present a case of a child with CCHS, mental retardation (MR), and HD who had general anesthesia while undergoing dental treatment.

CASE REPORT

A 4-year-old, 90-cm, 12-kg girl with CCHS, MR, and HD was treated under general anesthesia.

The patient was born at 41 weeks' gestation by vaginal delivery and diagnosed with CCHS because cyanosis appeared immediately after delivery. Oxygen saturation was unstable, and the patient had no ventilatory response to hypercapnia. At 3 months of age, the pa-

tient had a tracheotomy under general anesthesia, and she depended on mechanical ventilation during sleep. At 4 months of age, an intestinal resection was performed under general anesthesia for ileus because of HD.

The patient had stunted growth. She could not walk; she could only stand by taking hold of something, and usually moved with the assistance of a stroller.

The patient visited our hospital for treatment. At first we were treating her teeth under local anesthesia, but behavior management while conscious was very difficult. Because the patient moved significantly during dental treatment, we restrained her activity. During the dental treatment, the patient wailed and stopped breathing, and then cyanosis appeared. Therefore we could only treat her for a short time, and the patient had to visit our hospital many times. Her mother requested treatment under general anesthesia.

On the day before the operation, the patient entered our hospital with a ventilator, which she usually used. On the day of the operation, the patient entered the operation room at 9 AM without premedication. She did not cry, was not excited, and retained her composure. Her heart rate, blood pressure, and blood oxygen saturation were 93 beats/min, 121/82 mm Hg, and 98%, respectively. We connected her tracheotomy tube to a

Received November 14, 2003; accepted for publication April 28, 2004.

Address correspondence to Dr Hajime Ishibashi, Department of Anesthesiology, Nihon University School of Dentistry at Matsudo, 870-1, Sakaecho-Nishi 2, Matsudo, Chiba 271-8587, Japan; ishishash@masc.nihon-u.ac.jp.

Anesth Prog 51:102-104 2004
© 2004 by the American Dental Society of Anesthesiology

ISSN 0003-3006/04/\$9.50
SSDI 0003-3006(04)

semiclosed circuit anesthetic machine. After preoxygenation, slow induction was performed with 5% of sevoflurane without a muscular relaxant. Anesthesia was maintained with 0.5–1.5% sevoflurane in oxygen (3 L/min) and nitrous oxide (3 L/min) with controlled ventilation. Twelve teeth were filled with light curing resin, and 1 tooth was treated by the amputation of vital pulp. Before amputation of the vital pulp, local anesthesia was administered with 2% lidocaine and 1:200,000 epinephrine.

Intraoperatively at 10:10 AM, an arterial blood gas sample showed pH 7.457, PaO₂ 268.0 mm Hg, and PaCO₂ 27.9 mm Hg. The operation time was 2 hours and 20 minutes. After regaining consciousness and satisfactory spontaneous respiration, the patient returned to the ward at noon. The time from the end of the operation to her return to the ward was 18 minutes.

Supplemental oxygen via tracheotomy mask (3 L/min) continued in the ward. Her ECG and SpO₂ were monitored for 3 hours after returning to the ward. There was no problem after the operation.

The patient was discharged from our hospital the next day.

DISCUSSION

CCHS is a rare respiratory disorder characterized by normal ventilation when the patient is awake, but the patient has insufficient response to hypoxia and hypercapnia during sleep, even in the absence of pulmonary or neuromuscular diseases.¹ Mellins et al³ described the criteria for diagnosis of CCHS in 1970: (a) cyanosis is present on the first day of life; (b) primary disease of the heart, lungs, thoracic cage, and neuromuscular system can be excluded; (c) hypercapnia and hypoxemia can be easily eliminated in the neonatal period by assisted respiration; (d) alveolar hypoventilation is present in spite of such known stimuli to breathing as elevated PCO₂ and hydrogen ion concentration in the blood and the cerebrospinal fluid; and (e) the ventilatory response to inhaled CO₂ is reduced. Our patient was consistent with the criteria (ie, cyanosis appeared immediately after delivery, oxygen saturation was unstable, the patient had no ventilatory response to hypercapnia, and hypercapnia and hypoxemia were improved by mechanical ventilation). Therefore, she was diagnosed as having CCHS.

HD is a condition caused by the congenital absence of ganglion cells from the enteric nervous system, resulting in bowel obstruction ranging in severity from chronic severe constipation to complete obstruction and early neonatal death.¹ However, the patient we treated had survived because an intestinal resection was per-

formed under general anesthesia for ileus at 4 months of age.

Croaker et al¹ reported 46 cases of patients who have CCHS and HD, including 5 cases of their own, and they described that hypotonia and seizures have often been reported (in 13 of the 46 patients). Although these may be secondary to hypoxia, they could also represent a primary phenomenon. The inability to walk might not be a result of primary neuromuscular weakness with CCHS, but rather a secondary condition to hypoxia.

There were 18 deaths from among the 46 patients in the review in whom the outcome was known. They died between 10 days and 5.5 years. Nineteen of 46 patients were alive between 5 months and 7.5 years.¹ The patients with this association, therefore, are considered to have a poor prognosis for life.

Curiously, CCHS has been associated with several disorders classified as neurocristopathies—that is, aberrant phenotypes arising from a defect of migration or differentiation of neural crest cells.⁴ The most common neurocristopathy associated with CCHS is HD, with an incidence of 16–50% in CCHS patients.^{1,4} A combination of CCHS and HD, however, is very rare as there are only about 50 cases reported worldwide.^{1,2,5,6} Therefore our case in which a patient had general anesthesia while undergoing dental treatment was very rare. The anesthetic implications of this syndrome have not been reported to our knowledge. Therefore, the risk for anesthesia in these patients is unknown.

The cause of CCHS is unknown, but a genetic etiology is strongly suspected.⁷ There have been reports of CCHS in siblings,^{8,9} in female twins,¹⁰ and in mother-daughter relationships.⁷ In a larger study of several CCHS families, Weese-Mayer et al¹¹ found a suggestion of multifactorial inheritance in patients with CCHS with HD, but this was less strong in CCHS without HD. The family of our patient, however, had no CCHS, although the patient also had HD.

To date, the most effective therapy of CCHS has been assisted mechanical ventilation during sleep.² In fact, the patient had a tracheotomy under general anesthesia at 3 months of age, and she depended on mechanical ventilation during sleep.

It was not necessary to intubate the patient because a tracheotomy had already been performed. Therefore the induction of anesthesia was very easy and smooth.

Infants with CCHS are more sensitive to the respiratory depressant effects of opioids.¹² We were afraid that hypoventilation or apnea might continue after the operation because the effects of not only opioids but also preoperative sedatives, anxiolytics, muscular relaxants, and intravenous anesthetics are prolonged. Therefore we did not use these drugs and relied only on sevoflurane. The low blood solubility of sevoflurane is useful

for the rapid establishment of an anesthetic concentration and its lack of irritation of the airway. As a result the recovery was very short, only 18 minutes.

There was no trouble during the perioperative period. We safely performed general anesthesia and dental treatment on a girl who had CCHS with HD and MR.

REFERENCES

1. Croaker GDH, Shi E, Simpson E, Cartmill T, Cass DT. Congenital central hypoventilation syndrome and Hirschsprung's disease. *Arch Dis Child*. 1998;78:316-322.
2. Masumoto K, Arima T, Izaki T, et al. Ondine's Curse associated with Hirschsprung disease and ganglioneuroblastoma. *J Pediatr Gastroenterol Nutr*. 2002;34:83-86.
3. Mellins RB, Balfour HH Jr, Turino GM, Winters RW. Failure of automatic control of ventilation (Ondine's Curse). *Medicine*. 1970;49:487-504.
4. Bolk S, Angrist M, Xie J, et al. Endothelin-3 frameshift mutation in congenital central hypoventilation syndrome. *Nat Genet*. 1996;13:395-396.
5. Varma RR, Narayanankutty PK, Rajagopalan K, Rajeevan K. Hirschsprung's disease associated with Ondine's Curse. *Indian J Pediatr*. 2002;69:987-988.
6. Rohrer T, Trachsel D, Engelcke G, Hammer J. Congenital central hypoventilation syndrome associated with Hirschsprung's disease and neuroblastoma: case of multiple neurocristopathies. *Pediatr Pulmonol*. 2002;33:71-76.
7. Sritippayawan S, Hamutcu R, Kun SS, Ner Z, Ponce M, Keens TG. Mother-daughter transmission of congenital central hypoventilation syndrome. *Am J Respir Crit Care Med*. 2002;166:367-369.
8. Kerbl R, Litscher H, Grubbauer HM, et al. Congenital central hypoventilation syndrome (Ondine's Curse Syndrome) in two siblings: delayed diagnosis and successful noninvasive treatment. *Eur J Pediatr*. 1996;155:977-980.
9. Hamilton J, Bodurtha JN. Congenital central hypoventilation syndrome and Hirschsprung's disease in half sibs. *J Med Genet*. 1989;26:272-274.
10. Khalifa MM, Flavin MA, Wherrett BA. Congenital central hypoventilation syndrome in monozygotic twins. *J Pediatr*. 1988;113:853-855.
11. Weese-Mayer DE, Silvestri JM, Huffman AD, et al. Case/control family study of autonomic nervous system dysfunction in idiopathic congenital central hypoventilation syndrome. *Am J Med Genet*. 2001;100:237-245.
12. Brouwers MJA, Driessen JJ, Severijnen RSVM. Epidural analgesia in a newborn with Hirschsprung's disease, associated with congenital central hypoventilation syndrome. *Eur J Anaesthesiol*. 2000;17:751-753.